

This listing of claims will replace all prior versions, and listings, of claims in the application.

**I. Listing of Claims:**

1. (Previously Presented) A glycopeptide of the formula  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1 in which each dash represents a covalent bond; wherein the group  $A_1$  comprises a modified or unmodified  $\alpha$ -amino acid residue, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl, arylsulfonyl, guanidiny, carbamoyl, or xanthyl; where each of the groups  $A_2$  to  $A_7$  comprises a modified or unmodified  $\alpha$ -amino acid residue, whereby (i) the group  $A_1$  is linked to an amino group on the group  $A_2$ , (ii) each of the groups  $A_2$ ,  $A_4$  and  $A_6$  (bears an aromatic side chain, which aromatic side chains are cross-linked together by two or more covalent bonds, and (iii) the group  $A_7$  bears a terminal carboxyl, ester, amide, or N-substituted amide group;

and wherein one or more of the groups  $A_1$  to  $A_7$  is linked via a glycosidic bond to

one or more glycosidic groups each having one or more sugar residues; wherein at least one of said sugar residues is a disaccharide modified to bear one or more substituents of the formula  $YXR$ ,  $N^+(R_1)=CR_2R_3$ ,  $N=PR_1R_2R_3$ ,  $N^+R_1R_2R_3$  or  $P^+R_1R_2R_3$  in which the group  $Y$  is a single bond,  $O$ ,  $NR_1$  or  $S$ ; the group  $X$  is  $O$ ,  $NR_1$ ,  $S$ ,  $SO_2$ ,  $C(O)O$ ,  $C(O)S$ ,  $C(S)O$ ,  $C(S)S$ ,  $C(NR_1)O$ ,  $C(O)NR_1$ , or halo (in which case  $Y$  and  $R$  are absent); and  $R$ ,  $R_1$ ,  $R_2$ , and  $R_3$  are independently hydrogen, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl or arylsulfonyl; and any pharmaceutically acceptable salts thereof; provided that at least one of the substituents of the formula  $YXR$  is not hydroxyl;  $X$  and  $Y$  are not both  $O$ ;  $X$  and  $Y$  are not  $S$  and  $O$ , or  $O$  and  $S$ , respectively; and if two or more of said substituents are present, they can be the same or different; and

provided that when  $A_4$  is linked to a disaccharide having a glucose residue that bears an N-substituted aminohexose residue, then said glucose residue is modified to bear at least one of said substituents  $YXR$ ,  $N^+(R_1)=CR_2R_3$ ,  $N=PR_1R_2R_3$ ,  $N^+R_1R_2R_3$  or  $P^+R_1R_2R_3$ .

2. (Original) The glycopeptide of claim 1 in which said disaccharide comprises two hexose residues linked to  $A_4$  and wherein at least the hexose residue linked directly to  $A_4$  is modified to bear at least one of said substituents  $YXR$ ,  $N^+(R_1)=CR_2R_3$ ,  $N=PR_1R_2R$ ,  $N^+R_1R_2R_3$  or  $P^+R_1R_2R_3$ .
3. (Original) The glycopeptide of claim 2 in which said substituent is attached to the C6 position of said hexose residue linked directly to  $A_4$ .
4. (Original) The glycopeptide of claim 3 in which said hexose residue linked directly to  $A_4$  is glucose.
5. (Original) The glycopeptide of claim 4 in which at least one of said substituents is  $YXR$  wherein  $Y$  is a single bond and  $X$  is  $O$ ,  $NR_1$ ,  $S$  or  $SO_2$ .
6. (Original) The glycopeptide of claim 5 wherein  $X$  is  $NR_1$ .
7. (Original) The glycopeptide of claim 5 wherein  $X$  is  $S$ .
8. (Original) The glycopeptide of claim 5 wherein  $X$  is  $SO_2$ .
9. (Original) The glycopeptide of claim 5 wherein  $X$  is  $O$  and  $R$  is not  $H$ .
10. (Original) The glycopeptide of claim 4 wherein at least one of said substituents  $YXR$  is halogen.
11. (Previously Presented) The glycopeptide of claim 2 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.
12. (Previously Presented). The glycopeptide of claim 3 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.
13. (Previously Presented). The glycopeptide of claim 4 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.

14. (Previously Presented). The glycopeptide of claim 5 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.
15. (Previously Presented). The glycopeptide of claim 6 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.
16. (Previously Presented). The glycopeptide of claim 7 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.
17. (Previously Presented). The glycopeptide of claim 8 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.
18. (Previously Presented). The glycopeptide of claim 9 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.
19. (Previously Presented). The glycopeptide of claim 10 wherein  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , SEQ ID NO:1, form a dalbaheptide.
20. (Original) The glycopeptide of claim 11, wherein  $A_6$  in said dalbaheptide is linked via a glycosidic bond to one or more sugar residues.
21. (Original) The glycopeptide of claim 11 wherein the amino acids in said dalbaheptide are those in vancomycin.
22. (Original) The glycopeptide of claim 20 wherein  $A_1$ , which is N-methyl leucine, has been selectively removed and replaced with another of said groups  $A_1$ .
23. (Original) The glycopeptide of claim 2 in which the other hexose residue bears at least one of said substituents.
24. (Original) The glycopeptide of claim 3 in which the other hexose residue bears at least one of said substituents.
25. (Original) The glycopeptide of claim 4 in which the other hexose residue bears at least one of said substituents.

26. (Original) The glycopeptide of claim 5 in which the other hexose residue bears at least one of said substituents.
27. (Original) The glycopeptide of claim 6 in which the other hexose residue bears at least one of said substituents.
28. (Original) The glycopeptide of claim 7 in which the other hexose residue bears at least one of said substituents.
29. (Original) The glycopeptide of claim 8 in which the other hexose residue bears at least one of said substituents.
30. (Original) The glycopeptide of claim 9 in which the other hexose residue bears at least one of said substituents.
31. (Original) The glycopeptide of claim 10 in which the other hexose residue bears at least one of said substituents.
32. (Original) The glycopeptide of claim 11 in which the other hexose residue bears at least one of said substituents.
33. (Original) The glycopeptide of claim 12 in which the other hexose residue bears at least one of said substituents.
34. (Original) The glycopeptide of claims 13 in which the other hexose residue bears at least one of said substituents.
35. (Original) The glycopeptide of claims 14 in which the other hexose residue bears at least one of said substituents.
36. (Original) The glycopeptide of claim 23 wherein at least one of said substituents is YXR wherein Y is a single bond and X is O, NR<sub>1</sub>, S or SO<sub>2</sub>.
37. (Original) The glycopeptide of claim 36 wherein X is NR<sub>1</sub>.

38. (Original) The glycopeptide of claim 37 wherein said substituent is attached to C3 of said other hexose residue.

39. (Original) A chemical library comprising a plurality of glycopeptides, each of said glycopeptides having the formula  $A_1-A_2-A_3-A_4-A_5-A_6-A_7$ , in which each dash represents a covalent bond; wherein the group  $A_1$  comprises a modified or unmodified  $\alpha$ -amino acid residue, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl, arylsulfonyl, guanidiny, carbamoyl, or xanthyl; where each of the groups  $A_2$  to  $A_7$  comprises a modified or unmodified  $\alpha$ -amino acid residue, whereby (i) the group  $A_1$  is linked to an amino group on the group  $A_2$ , (ii) each of the groups  $A_2$ ,  $A_4$  and  $A_6$  bears an aromatic side chain, which aromatic side chains are cross-linked together by two or more covalent bonds, and (iii) the group  $A_7$  bears a terminal carboxyl, ester, amide, or N-substituted amide group;

and wherein one or more of the groups  $A_1$  to  $A_7$  is linked via a glycosidic bond to one or more glycosidic groups each having one or more sugar residues; wherein at least one of said sugar residues is a disaccharide modified to bear one or more substituents of the formula  $YXR$ ,  $N^+(R_1)=CR_2R_3$ ,  $N=PR_1R_2R_3$ ,  $N^+R_1R_2R_3$  or  $P^+R_1R_2R_3$  in which the group  $Y$  is a single bond,  $O$ ,  $NR_1$  or  $S$ ; the group  $X$  is  $O$ ,  $NR_1$ ,  $S$ ,  $SO_2$ ,  $C(O)O$ ,  $C(O)S$ ,  $C(S)O$ ,  $C(S)S$ ,  $C(NR_1)O$ ,  $C(O)NR_1$ , or halo (in which case  $Y$  and  $R$  are absent); and  $R$ ,  $R_1$ ,  $R_2$ , and  $R_3$  are independently hydrogen, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl or arylsulfonyl; and any pharmaceutically acceptable salts thereof; provided that at least one of the substituents of the formula  $YXR$  is not hydroxyl;  $X$  and  $Y$  are not both  $O$ ;  $X$  and  $Y$  are not  $S$  and  $O$ , or  $O$  and  $S$ , respectively; and if two or more of said substituents are present, they can be the same or different; and

provided that when  $A_4$  is linked to a disaccharide having a glucose residue that bears an N-substituted aminohexose residue, then said glucose residue is modified to bear at least one of said substituents  $YXR$ ,  $N^+(R_1)=CR_2R_3$ ,  $N=PR_1R_2R_3$ ,  $N^+R_1R_2R_3$  or  $P^+R_1R_2R_3$ .

40. (Original) The chemical library of claim 39 wherein  $A_1$   $A_1-A_2-A_3-A_4-A_5-A_6-A_7$  form a dalbaheptide and wherein said disaccharide comprises two hexose residues linked to  $A_4$

and wherein at least the hexose residue linked directly to A<sub>4</sub> is modified to bear said substiruent at the C6 position.

41. (Original) The chemical library of claim 40 wherein the other hexose residue bears a group YXR in which Y is a single bond and X is NR<sub>1</sub>.

Claims 42-49 (Cancelled)

50. (Original) A method for producing the chemical library of claim 39, said method comprising at least two steps in each of which a substituent is introduced on a glycopeptide.

51. (Original) The method of claim 50 wherein at least one of said two steps comprises introducing a substituent on the 6-position of a hexose residue directly linked to A<sub>4</sub>.

52. (Original) The method of claim 51 wherein the other of said at least two steps comprises introducing an N-substituent on an aminohexose residue bonded to said hexose residue directly linked to A<sub>4</sub>.

53. (Original) The method of claim 52 wherein said hexose residue directly linked to A<sub>4</sub> is a glucose residue.

54. (Original) The method of claim 51 wherein A<sub>1</sub>-A<sub>2</sub>-A<sub>3</sub>-A<sub>4</sub>-A<sub>5</sub>-A<sub>6</sub>-A<sub>7</sub> form a dalbaheptide.

55. (Original) The method of claim 54 wherein the amino acids in said dalbaheptide are those in vancomycin.

56. (Original) The method of claim 55 wherein A<sub>1</sub> which is N-methyl leucine, has been selectively removed and replaced with another of said groups A<sub>1</sub>.

57. (Original) A method of preparing a glycopeptide comprising:  
(a) selecting: (i) an aglycone that is soluble in one or more organic solvents, is derived from a glycopeptide antibiotic, and which aglycone has exactly one free phenolic hydroxyl group; and (ii) a protected first glycosyl donor;

- (b) allowing a first non-enzymatic glycosylation reaction to proceed in an organic solvent such that a first glycosidic bond is formed, which links said free phenolic hydroxyl group to the anomeric carbon of the first glycosyl donor to provide a pseudoaglycone having a protected first glycosyl residue;
- (c) selectively removing one protecting group from the first glycosyl residue to provide a pseudoaglycone bearing exactly one free hydroxyl group on the first glycosyl residue;
- (d) selecting a second protected glycosyl donor; and
- (e) allowing a second non-enzymatic glycosylation reaction to proceed in an organic solvent such that a second glycosidic bond is formed, which links said free hydroxyl group on the pseudoaglycone to the anomeric carbon of the second glycosyl donor.

Claims 58 – 73 (Cancelled)

74. (Original) A method for producing the chemical library of claim 39; said method comprising at least two steps, wherein at least one of said at least two steps comprises a glycosylation reaction which introduces a substituted sugar residue.

75. (Original) The method of claim 74 in which  $A_1$  to  $A_7$  are linked sequentially by peptide bonds and cross-linked as in a dalbaheptide.

76. (Original) The method of claim 75 in which said glycosylation reaction links said substituted sugar residue to an  $A_4$  residue of an aglycone.

77. (Original) The method of claim 76 in which said glycosylation reaction links said substituted sugar residue to a sugar residue of a pseudoaglycone, wherein said sugar residue of a pseudoaglycone is linked to an  $A_4$  residue of the pseudoaglycone.

78. (Original) The method of claim 76 in which a second glycosylation reaction links a second substituted sugar residue to said substituted sugar residue.

79. (Original) The method of claim 77 in which  $AI$  is a modified or unmodified  $\alpha$ -amino acid residue, and in which  $A_1$  to  $A_7$  are linked sequentially by peptide bonds and cross-linked so as to have the structure of a dalbaheptide.



80. (Original) The method of claim 78 in which  $A_1$  is a modified or unmodified  $\alpha$ -amino acid residue, and in which  $A_1$  to  $A_7$  are linked sequentially by peptide bonds and cross-linked so as to have the structure of a dalbaheptide.

81. (Original) The method of claim 77 in which the structures and interconnections of  $A_1$  to  $A_7$  are those found in vancomycin.

82. (Original) The method of claim 81 in which a glycosyl donor bearing an activated anomeric sulfoxide group is employed in each glycosylation reaction.

Claims 83-101 (Cancelled)

102. (Original) A glycopeptide antibiotic bearing at least one disaccharide group, said disaccharide group comprising two saccharide groups, a first of said saccharide groups bearing at least one amino or substituted amino group, and a second of said saccharide groups modified to bear at least one substituent which is not hydroxyl, or a pharmaceutically acceptable salt thereof.

103. (Original) The glycopeptide antibiotic of claim 102 wherein the second of said saccharide groups is glucose modified to bear at least one substituent which is not hydroxyl at the C6 position of said glucose.

104. (Original) The glycopeptide antibiotic of claim 103 which is vancomycin modified to bear at least one substituent which is not hydroxyl at the C6 position of said glucose.

105. (Original) The glycopeptide antibiotic of claim 104 wherein said at least one substituent which is not hydroxyl at the C6 position of said glucose is amino.

106. (Original) The glycopeptide antibiotic of claim 105 wherein the first of said saccharide groups bears at least one substituted amino group.

107. (Original) The glycopeptide antibiotic of claim 106 wherein said substituted amino group is  $NR_1H$  wherein  $R_1$  bears one or more alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic or substituted heterocyclic groups.



108. (Original) The glycopeptide antibiotic of claim 107 wherein at least one of said substituted alkyl groups is aralkyl.

109. (Original) The glycopeptide antibiotic of claim 107 wherein at least one of said substituted aryl groups is aralkyloxy substituted aryl.

110. (Original) The glycopeptide antibiotic of claim 107 wherein at least one of said substituted aryl groups is halo substituted aryl.

111. (Original) The glycopeptide antibiotic of claim 102 wherein the first of said saccharide groups bears at least one substituted amino group.

112. (Original) The glycopeptide antibiotic of claim 111 wherein said substituted amino group is  $\text{NR}_1\text{H}$  wherein  $\text{R}_1$  bears one or more alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic or substituted heterocyclic groups.

113. (Original) The glycopeptide antibiotic of claim 112 wherein at least one of said substituted alkyl groups is aralkyl.

114. (Original) The glycopeptide antibiotic of claim 112 wherein at least one of said substituted aryl groups is aralkyloxy substituted aryl.

115. (Original) The glycopeptide antibiotic of claim 112 wherein at least one of said substituted aryl groups is halo substituted aryl.

116. (Original) The glycopeptide antibiotic of claim 112 wherein said at least one substituent which is not hydroxyl is amino.